NDA 022195/S-010
NDA 022207/S-005

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT

Hikma Pharmaceuticals USA Inc.
1809 Wilson Road
Columbus, OH 43228

Attention: Tae Kim, PhD
Director, Clinical Development

Dear Dr. Kim:

Please refer to your supplemental new drug applications (sNDAs) dated and received March 23, 2015, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for:

NDA Number	Supplement Number	Product
022195	S-010	Morphine sulfate oral solution
022207	S-005	Morphine sulfate tablets

We acknowledge receipt of your amendments dated December 2, 2020, which constituted a complete response to our January 21, 2016, action letter.

These Prior Approval supplemental new drug applications provide for changes to the INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, USE IN SPECIFIC POPULATIONS, and CLINICAL PHARMACOLOGY sections of the prescribing information based on the results of pediatric study *A Multicenter, Open-Label, Safety and Pharmacokinetic Study of Oral Morphine Sulfate Administration in Pediatric Subjects 2 years old through 17 years old with Postoperative Pain*, submitted in fulfillment of postmarketing requirement (PMR) 204-3.

APPROVAL & LABELING

We have completed our review of these applications, as amended. These are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

The Instructions for Use (IFU) document does not include the necessary graphics. We remind you of your commitment to submit a PAS to revise the IFU to include graphics corresponding to the step-by-step instructions prior to marketing the product.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Instructions for Use, and Medication Guide), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.[2]

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved NDA 022195/S-010 and NDA**

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

022207/S-005." Approval of this submission by FDA is not required before the labeling is used.

PROPRIETARY NAME

If you intend to have a proprietary name for this product, the name and its use in the labeling must conform to the specifications under 21 CFR 201.10 and 201.15. We recommend that you submit a request for a proposed proprietary name review. (See the guidance for industry *Contents of a Complete Submission for the Evaluation of Proprietary Names* and *PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2018 through 2022*.)

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your applications, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENT (PMR)

On May 17, 2010, FDA issued a letter releasing you of your previous PREA requirements, and replacing them with two new postmarketing requirements.

We have received your submissions dated March 23, 2015, and December 2, 2020, containing the final study reports for the following postmarketing requirement listed in the May 17, 2010, letter:

204-3 Deferred pediatric study of pharmacokinetics and safety under PREA for the treatment of moderate to severe pain where an opioid analgesic is appropriate in pediatric patients ages 2 to 17 years

We have reviewed your submissions and conclude that the above requirement was fulfilled.

We also refer to our Advice letter dated May 27, 2021, issued under IND 075041, to request that you submit a toxicological risk assessment for the safety of the drug product excipients in the drug product you intend to study in pediatric patients less than

2 years of age. This assessment should be submitted as soon as possible because an adequate justification for the safety of the dosage form will be necessary to support your clinical study planned to address PMR 204-4.

We remind you that there is a postmarketing requirement listed in the in the May 17, 2010, letter that PMR 204-4 is still outstanding.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[3]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

If you have any questions, contact Sandy Truong, Regulatory Project Manager, at 301-796-5719.

Sincerely,

{See appended electronic signature page}

Rigoberto Roca, MD
Director
Division of Anesthesiology, Addiction Medicine, and Pain Medicine
Office of Neuroscience
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - Instructions for Use
- Carton and Container Labeling

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

RIGOBERTO A ROCA
06/02/2021 05:00:56 PM